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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,184	06/13/2007	Satoru Yamagami	01125_1000	3525

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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
10/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,184	YAMAGAMI ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08/18/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *6 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :08/18/20006, 06/13/2007, 08/04/2008.

DETAILED ACTION

The preliminary amendment filed on August 18, 2006, has been received.

Claims 1-15 are pending in this application and were examined on their merits.

Specification

The amendment filed 08/18/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

On Page 7, please replace paragraph [0024] with the following:

-- The number of cells dripped onto the collagen sheet is desirably two or more times the normal density of endothelial cells (3,000 cells/mm2), with twice (6,000 cells/$mm^{2)}$ to [[10]] 20 times (60,000 cells/$mm^{2)}$ being preferred.--

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objection

Claims 6 and 11 are objected to because of the following informalities:

In claim 6 line 2, the word "layer" is unnecessary.

In claim 11 line 3, delete "a" and insert --the--.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-8, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Amano et al. (in IDS, 2002, Journal of Japanese Ophthalmologic Society, Vol. 106, No.12, p.805-836) as evidenced by Newsome et al. (Invest. Ophthalmol. Vis. Sci.,1982, Vol. 22, p.376-381).

Claims 1 and 2 are drawn to a laminate comprising a transparent type I collagen sheet and a cultured layer of human corneal endothelial cells provided on said sheet, the transparency of type I collagen sheet is maintained.

Claims 6-8 and 10 are drawn to a method for manufacturing a laminate of cultured human corneal endothelial cells, comprising preparing a transparent type I collagen sheet, and culturing human corneal endothelial cells on said sheet to form a cultured layer of human corneal endothelial, the human corneal endothelial cells are cultured on a transparent type I collagen sheet that has been coated with an adhesive factor, and the human corneal endothelial cells are cultured after providing a culture solution containing human corneal endothelial cells on a transparent type I collagen sheet and applying centrifuge force in the direction of said transparent type I collagen sheet.

Amano et al. disclose a method for manufacturing a laminate of cultured human corneal endothelial cells, comprising preparing a transparent type I collagen sheet, and culturing human corneal endothelial cells on said sheet to form a cultured layer of human corneal endothelial (p.807 1st column 2nd paragraph lines 1-5), the human corneal endothelial cells are cultured on a transparent type I collagen sheet that has been coated with an adhesive factor (p.806 Abstract 1st column end paragraph lines and 2nd column lines 1-3), the human corneal endothelial cells are cultured after providing a culture solution containing human corneal endothelial cells on a transparent type I collagen sheet and applying centrifuge force in the direction of said transparent type I collagen sheet, using a cell culturing solution comprising fetal bovine serum, growth factor (p.806 Abstract 1st column end paragraph continued to 2nd column 2nd lines 1-3 and p.807 1st column 2nd paragraph lines 2-5).

Amano et al. also disclose reconstructed cornea (a laminate) comprising human corneal stroma (transparent type I collagen sheet) and a cultured layer of human corneal endothelial cells provided on said sheet, the transparency of type I collagen sheet is maintained (p.807 1st column 2nd paragraph lines 1-5 and 14-15). It must be noted that human corneal stroma contains collagen type I (see Newsome et al. Newsome et al. Abstract).

Amano et al. therefore clearly anticipate the claimed laminate and method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amano et al. (in IDS, 2002, Journal of Japanese Ophthalmologic Society, Vol. 106, No.12, p.805-836) in view of Civerchia (US Patent No. 5,716,633) and further in view of Miyata et al. (Cornea, 2001, Vol. 20. No.1, p.59-63) and Inoue et al. (Invest. Ophthalmol. Vis. Sci., 1993, Vol. 34, No. 7, 2313-2315).

Claims 1-5 are drawn to a laminate comprising a transparent type I collagen sheet and a cultured layer of human corneal endothelial cells provided on said sheet, the transparency of type I collagen sheet is maintained, transparent type I collagen sheet has an adhesive factor or bioadhesive on the opposite side from the cultured layer of human corneal endothelial cells and between the transparent type I collagen sheet and cultured layer of human corneal endothelial cells, and the adhesive factor is human plasma fibronectin.

Claims 6-15 are drawn to a method for manufacturing a laminate of cultured human corneal endothelial cells, comprising preparing a transparent type I collagen sheet, and culturing human corneal endothelial cells on said sheet to form a cultured layer of human corneal endothelial, the human corneal endothelial cells are cultured on a transparent type I collagen sheet that has been coated with an adhesive factor, the

adhesive factor is human plasma fibronectin, the human corneal endothelial cells are cultured after providing a culture solution containing human corneal endothelial cells on a transparent type I collagen sheet and applying centrifuge force in the direction of said transparent type I collagen sheet, the concentration of human corneal endothelial cells in the culture solution is set to within a range of from $1X10^5$ to $1X10^7$ cells/ml, human corneal endothelial cells have been passaged for 2 to 10 generations, human corneal endothelial cells are cultured under conditions of 37°C and 10 % CO_2, using a cell culturing solution comprising fetal bovine serum, growth factor, and hyaluronic acid in a medium of low glucose concentration.

As mentioned immediately above, Amano et al. teach a method for manufacturing a laminate of cultured human corneal endothelial cells, comprising preparing a transparent type I collagen sheet, and culturing human corneal endothelial cells on said sheet to form a cultured layer of human corneal endothelial (p.807 1st column 2nd paragraph lines 1-5), the human corneal endothelial cells are cultured on a transparent type I collagen sheet that has been coated with an adhesive factor (p.806 Abstract 1st column end paragraph lines and 2nd column lines 1-3), the human corneal endothelial cells are cultured after providing a culture solution containing human corneal endothelial cells on a transparent type I collagen sheet and applying centrifuge force in the direction of said transparent type I collagen sheet, using a cell culturing solution comprising fetal bovine serum, growth factor (p.806 Abstract 1st column end paragraph continued to 2nd column 2nd lines 1-3 and p.807 1st column 2nd paragraph lines 2-5).

Amano et al. teach reconstructed cornea (a laminate) comprising a transparent type I collagen sheet and a cultured layer of human corneal endothelial cells provided on said sheet, the transparency of type I collagen sheet is maintained under physiological condition (p.807 1st column 2nd paragraph lines 1-5 and 14-15).

Amano et al. do not teach using human plasma fibronectin, human corneal endothelial cells are cultured under conditions of 37°C and 10 % CO_2, in a medium of low glucose concentration, cells have been passaged for 2 to 10 generations, and hyaluronic acid. However, Civerchia teaches fibronectin supports the attachment and growth of cells and enhances corneal epithelial cell growth (column 11 lines 42-45 and column 15 Example V lines 62-63).

Miyata et al. teaches human corneal endothelial cells or HCEC cultured under conditions of 37°C and 10 % CO_2, in a medium of low glucose concentration (Dulbecco modified Eagle medium or DMEM) (p.59 2nd column Material & Methods, lines 2-3, and 6-9) and human corneal endothelial cells have been passaged for 2 to 10 generations (p.62 1st column 1st paragraph line 3).

Inoue et al. teach hyaluronic acid or HA stimulates corneal epithelial and promotes wound healing (Abstract).

Therefore, in view of the above teachings, a person of ordinary skill at the time the invention was made, would have been able to apply the prior art teaching in the method of Amano et al. and to culture human corneal endothelial cells or HCEC under conditions of 37°C and 10 % CO_2, in a medium of low glucose concentration with hyaluronic acid according to the teachings of Miyata et al. and Inoue et al. in order to

provide a method for manufacturing a laminate of cultured human corneal endothelial cells and a laminate with a reasonable expectation of success, because Miyata et al. teach culturing human corneal endothelial cells or HCEC under conditions of 37°C and 10 % CO_2, in a medium of low glucose concentration and because Inoue et al. teach hyaluronic acid or HA stimulates corneal epithelial and promotes wound healing.

Moreover, a person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the adhesive factor in the method as taught by Amano et al. with fibronectin according to the teachings of Civerchia in order to provide a method for manufacturing a laminate of cultured human corneal endothelial cells and a laminate with a reasonable expectation of success, because Civerchia teaches fibronectin supports the attachment and growth of cells and enhances corneal epithelial cell growth.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on IFP.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651